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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,977	01/06/2000	PETER C. BROOKS	13761-727	2450

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 05/13/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/478,977

Applicant(s)

BROOKS ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6, 10-18, 20-25, 27-30, 32-34, 36-38 and 40-64 is/are pending in the application.
- 4a) Of the above claim(s) 20-25, 27-30, 32-34, 36-38 and 40-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6 and 10-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

1. The request filed on October 23, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/478,977 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 1-4, 6, 10-18, 20-25, 27-30, 32-34, 36-38 and 40-64 are pending.

Claims 6 and 11 have been amended.

Claims 20-25, 27-30, 32-34, 36-38 and 40-64, drawn to non-elected inventions are withdrawn from examination.

Claims 1-4, 6 and 10-18 are examined on the merits.

Priority

3. Provisional documents 60/114,877 (filed January 6, 1999), 60/114,878 (filed January 6, 1999), 60/152,496 (filed September 2, 1999) and 60/143,534 (filed July 13, 1999) from which Applicants request priority benefit were reviewed by the Examiner. Claims 1-4, 6, 10 and 12-18 are afforded the effective filing date of January 6, 1999. None of the provisional applications simultaneously reference all three monoclonal antibodies, hence claim 11 is afforded the effective filing date of January 6, 2000. Applicants are reminded that a claim as a whole has only one effective filing date.

Specification

4. The disclosure is objected to because of the following informality: on page 3, line 16 the term "effect" should be replaced with the term "affect". In the context of the sentence the improper verb has been used.

Correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 11 is are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of antibodies HU177, HUVIV26 and XL313. It is not clear that antibodies possessing the identical properties of these instant antibodies are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of an antibody capable of binding a specific epitope is an unpredictable event. Although applicant has provided a written description of a method for generating and isolating the specified monoclonal antibodies, this method will not

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necessarily reproduce antibodies and which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive antibodies identical to those claimed. Undue experimentation would be required to screen all of the possible antibody species to obtain the claimed antibodies.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibodies, a suitable deposit of the molecules designated as HU177, HUIV26 and XL313 for patent purposes, evidence of public availability of the claimed cell lines or evidence of the reproducibility without undue experimentation of the claimed cell lines, is required.

Applicants have not made a referral to the deposit of the antibodies in the specification. There is insufficient assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposits are made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is

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necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

7. Claims 1-4, 6, 10 and 12-18 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antagonists, designated monoclonal antibodies, HU177, HUIV26 and XL313 binding denatured collagen for the inhibition of angiogenesis, does not reasonably provide enablement for a host of antagonists, such as an oligonucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants' specification contains examples and figures that provide evidence monoclonal antibodies, HU177, HUIV26 and XL313 are capable of inhibiting angiogenesis. This enabling disclosure provides evidence only of the specified antagonists capable of arresting angiogenesis. Applicants have not provided any evidence that suggests that other monoclonal antibodies, polyclonal antibodies, non-peptidic compounds, cyclic peptides or oligonucleotides would have the same inhibitory effect. A number of antibodies may possess a high affinity for the denatured collagens but not be effective in inhibiting angiogenesis. One of ordinary skill in the art could screen for effective antibody antagonists, but that would be burdensome considering the number of antibodies that possibly bind the broadly claimed collagen of claims 1-4 and specifically denatured collagen, type I. The specification only discloses three monoclonal antibodies effective in binding denatured collagen and consequently

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inhibiting angiogenesis and does not disclose any oligonucleotides or other antibodies effective in inhibiting angiogenesis.

Tennant et al. (Curr. Oncol. Rep. 2(1): 11-16, January 2000) has recapitulated the art known fact there are numerous angiogenesis inhibitors capable of targeting neovascular development. These inhibitors have been divided into five distinct categories based upon their target activity, see abstract. However, there exists a number of potential antiangiogenic compounds in development for which the mechanism of angiogenesis inhibition is unknown, see page 14, column 1, paragraph 2. Applicants' disclosure has only provided evidence that three specific antibodies are capable of binding denatured collagen thereby inhibiting angiogenesis. Moreover, as set forth by Tennant many potential antiangiogenic inhibitors exists but testing (namely clinical) involved in determining whether an agent has sufficient activity is painstaking and arduous, see entire article.

Applicants' claims are not commensurate in scope with what is enabled within the specification. And while Applicants do not have to provide astonishing results to the Office there should be a representative number of species encompassed by a broad claim/ genus. It would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the infinite number of antagonists that could possibly inhibit angiogenesis via binding of denatured collagen.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9 Claims 1-4, 6 and 10-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "denatured collagen" in claims 1-4, 6 and 10-18 is vague and indefinite. It is not clear by what means the collagen was denatured. Moreover it is not clear if the collagen chemically or structurally denatured. It is not clear if the denatured collagen conformationally consists of epitopes not exposed in native collagen or how it is different from native collagen. Accordingly, the metes and bound of the claims cannot be determined.

b. Claims 1-4 are vague and indefinite in the recitations "collagen" and "collagens". It is art known that the collagen superfamily now includes more than 20 collagen types with altogether at least 38 distinct polypeptide chains, and more than 15 additional proteins that have collagen-like domains. It is not clear from the claims which type of collagen the claims embrace.

c. Claim 1 is vague and indefinite in the recitation "substantially reduced affinity". The claim does not clarify what is regarded as limited affinity or what this reduced affinity is compared to. The metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Brooks et al. (J. Clin. Invest. 96: 1815-1822, October 1995/ IDS reference C2, Paper number 9), as evidenced by Brooks et al. (Cell 85: 683-693, May 31, 1996). Brooks (1995) discloses monoclonal antibody LM609, a $\alpha v \beta 3$ antagonist that blocks angiogenesis, see abstract, page 1817, second column, third paragraph. $\alpha v \beta 3$ fails to bind native collagen, but does interact with proteolyzed collagen, see Brooks (1996), page 683, column 2, Results section, third sentence; page 690, first column, first full paragraph. The specification asserts that the claimed antagonist is capable of binding both denatured or proteolyzed collagens, see page 4, lines 5-8 of instant specification. It is the Examiner's position bearing in mind the indefiniteness of the claim that the conformation of both denatured and proteolyzed forms of collagen expose epitopes not available in the native form of collagen. Inherently, the disclosed monoclonal antibody, which interacts with $\alpha v \beta 3$, would invariably bind denatured collagen type-I and native collagen with reduced affinity.


11. Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by Petitclerc et al. (Cancer Research 59:2724-2730, June 1, 1999). Petitclerc discloses a monoclonal antibody designated as Mab HU177, which is directed to denatured collagens. It is reasonable to conclude that the disclosed monoclonal antibody has the same binding specificity of Applicants' claimed antagonist.

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12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


ALANA HARRIS
PATENT EXAMINER
Alana M. Harris, Ph.D.
May 11, 2003